International Journal of Environment, Ecology, Family and Urban Studies (IJEEFUS)
ISSN (P): 2250-0065; ISSN (E): 2321-0109
Vol. 8, Issue 3, Jun 2018, 25-34

AETIOLOGY OF MILD AND SERIOUS INTELLECTUAL DISABILITIES/MR WITHOUT ANY IDENTIFIED GENETIC CAUSE

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ABSTRACT

The present study was designed to find etiology of non-genetic ID/MR and evaluated the contribution of demographic, prenatal, perinatal and neonatal factors to the prevalence of intellectual disability among individuals aged 10–17 years in Himachal Pradesh. This study explored the utility of subdividing mental retardation firstly on the basis of IQ and then further on the basis of presence or absence of neurological disorders. Kamat's Binet test was performed for dividing cases into mild (IQ=50-55 to 70) and serious (IQ=50-55-<20-25) These cases were further divided in to isolated and cases with other neurological abnormalities for eradicating the effects of these disorders on various degrees of mental retardation. This study concluded that prevention of mild retardation requires anticipation of some risk factors such as low maternal education, maternal history of pregnancy loss, lack of prenatal care, neonatal diarrhoea and neonatal infection, but serious cases are less compatible to the factor, neonatal diarrhoea. These risk factors found to be associated with MR, implied preventative strategies that could lessen the frequency of intellectual disability/ MR in children.

KEYWORDS: IQ Testing, Maternal Education, Maternal History of Pregnancy Loss, Lack of Prenatal Care & Neonatal Infection

Received: Apr 09, 2018; **Accepted:** Apr 30, 2018; **Published:** May 09, 2018; **Paper Id.:** IJEEFUSJUN20183

Original Article

INTRODUCTION

Intellectual disability (ID), earlier known as mental retardation is a lifelong cognitive impairment characterized by sub-average intellectual functioning and adaptive behavior, as articulated in theoretical, communal and useful adaptive skill that emerges before the age of 18 years (Reichenberg et al. 2017). Its prevalence has been estimated to be 1-3% (Maulik et al. 2011; Shevell et al. 2003). Depending upon etiology, ID is categorized into genetic or non-genetic. Genetic ID account for 30% to 50% of all ID cases (Curry et al.1997; de Vries et al. 2005), on the other hand, the causes of non-genetic ID are not fully identified. In particular, there is a scarcity of population-based studies for unraveling the unidentified causes, on the outcomes of complications in pregnancy, labor and the neonatal period (Lee et al. 2013). The present study is focussed on ascertaining the causes of non-genetic ID and prior to the study, a list of risk factors known to be associated with intellectual disability was drawn up from pertinent available literature to reduce the downfalls of afterward testing (Mwaniki et al. 2012; UNICEF 2004). In etiological studies, classifying mental retardation exclusively on the basis of IQ is unreliable so in the present investigation, criteria in addition to IQ is used by considering this notion that risk factors for mental retardation may be different for children who also have other developmental or other neurological conditions and for children who have only mental retardation. In addition to it investigators questioned this postulation or focussed

specifically on those children with ID/ MR of unknown cause which is rarely questioned in previous studies. We report here an investigation to assess the prevalence of certain demographic, prenatal, perinatal and neonatal risk factors of children with mild and serious MR (single term used for moderate, severe and profound cases) of unidentified cause among the total population of 150 cases.

METHODOLOGY

The data for present work included a case-control study of intellectual disability/MR among 150 selected individuals from the population of Himachal Pradesh. To limit the pitfalls of afterward testing, ahead of reviewing the dataset, a questionnaire was structured for abstracting information about potential risk factors which were selected stringently according to recent literature. The questionnaire was translated to Pahari dialect to have a excellent reliability and validity. The control subjects of age group were selected randomly from the same region. Kamat's Binet test of intelligence was performed for assessing the intelligence quotient and all MR cases were classified into mild, moderate, severe and profound individuals having IQ values as 50-55 to 70 (mild), 35-40 to 50-55 (moderate), 20-25 to 35-40 (severe) and <20-25 (profound). But in the present study, all cases with intellectual disabilities were categorized into mild and serious, since these categories proved to have different risk factor profiles, these were subsequently divided on the basis of presence or absence of other neurological abnormalities i.e microcephaly, epilepsy, hearing impairments and visual impairments.The cases with isolated MR were not known to have either of these abnormalities. The control subjects did not have any of the neurological abnormalities incorporated in our depiction. The selected a priori as potential risk factors were categorized into demographic, prenatal, perinatal and neonatal factors

Data Analysis

Chi-square test was used to find the significant association between various degrees of MR and potential risk factors both in isolated cases and cases with other neurological abnormalities. χ^2 values below 0.05 were taken as significant.

RESULTS

In the present investigation, a total of 150 MR with mean age 14.5 years, were screened to find an association between MR and various potential risk factors. Males outnumbered as compared to females with sex ratio as 2.6:1. Most of the cases (58%) had either of other neurological conditions. Cases with serious MR were more likely to have other neurological conditions (71.43%) as compared to mild MR (53.91%). The disparity among subgroups of MR cases was more prominent when were subdivided into two groups based on the occurrence of other neurological abnormalities. Maternal education, maternal history of pregnancy loss, lack of prenatal care and neonatal infection were associated with MR despite any subdivision. We reported that most of the factors influencing mild ID were similar to the controls but the factors influencing serious ID differed from both mild and normal cases.

Isolated Cases

Isolated MR cases were found to be predominantly associated with low maternal education, maternal history of pregnancy loss, hypertension during pregnancy, lack of prenatal care, neonatal diarrhea and neonatal infection. Mild isolated cases were exceptionally associated with hypertension during pregnancy and serious cases had shown association with difficult birth but not with neonatal diarrhea.

Cases with Other Neurological Conditions

MR cases with other neurological conditions also showed same associations as by isolated except difficult birth showed an association but not found to be associated with hypertension during pregnancy. Mild MR cases with other neurological conditions showed associations with hypertension during pregnancy and maternal tobacco use. But serious MR cases had shown the same associations as by MR cases with other neurological conditions except for difficult birth which was found to be negatively associated with intellectual disability/MR.

DISCUSSIONS

Causes of mental retardation are heterogeneous and elusive so it is one of the most complicated categories to document epidemiologically (Richmond et al. 1983). Ascertaining the causes of mental retardation in developing countries is difficult due to the dearth of indicative services and regularly collected health data. Very fewer children with cognitive disabilities had received educational or medical services. In spite of this authors were able to get information regarding potential risk factors in populations missing universal wellbeing care and regular data collection programmes. Our results suggested that most serious ID is a distinctive situation and represents the low extreme of the customary allocation of intelligence ((Reichenberg et al. 2017). Like previous studies, we found differences in the impact of demographic and factors from consecutive epochs of fetal and child development (prenatal, perinatal and neonatal) on the occurrence of mild and serious mental retardation (Drews et al. 1995; Durkin et al. 2000; Martindale 1980; Rantakallio 1987). The results of this epidemiologic survey carried out, are in agreement with many previous studies done so far (Belmont 1986; Bhushan et al. 1993; Narayanan 1981). Maternal education was found to be significantly associated all degrees of MR but paternal education did not show any association. This illustrates that education of mother is more imperative for healthy rearing which can help in plummeting the diseases load. There are many reports of a higher rate of ID in the infants of hypertensive mothers (Korkman et al. 1994; Szymonowicz and Yu, 1987), while a study found similar rate of disability of mothers with or without hypertension during pregnancy (Van Zeban der Aa et al. 1986) but present study is in contrast to these studies with no any associations with all subgroups and is in line with study done by Gray et al. in 1998.

Epidemiological associations for isolated mild mental retardation were almost similar to those of isolated severe mental retardation and mild mental retardation with other neurological conditions was similar to severe mental retardation with other neurological condition. Our results support the conception that both isolated MR and MR with other neurological conditions are influenced by demographic, prenatal and neonatal risk factors which are in contrast with studies done so far (Kushlick and Blunden 1974; Zigler, 1967), in which isolated MR was influenced by demographic factors and MR with other neurological conditions by pathological risk factors. The present study suggested that prevention of any of subgroups of intellectual disability/ MR would require preclusion of demographic factor of low maternal education, prenatal factors like lack of prenatal care and neonatal infection. Likewise, many previous studies showed significant associations of these risk factors with intellectual disability/ MR (Decoufle and Boyle 1995; Drews et al. 1995, 1996; Durkin et al. 2000; Yeargin-Allsopp et al. 1995; UNICEF 2012). Males were predominant in all subgroups, which showed uniformity with many previous studies (Lai et al. 2012; Reddy et al. 2018; Singhi Pratibha et al. 2002; Srivatsava et al. 1992; Van Naarden et al.2015). Mild isolated cases were found to be associated with low maternal education, lack of prenatal care, neonatal diarrhea, neonatal infection but be at variance from isolated MR cases in not showing any association with maternal hypertension during pregnancy. This finding is consistent with studies of mild mental retardation in European and North American studies (Stein and Susser 1984; Haworth et al. 2017). Whereas serious isolated cases

have shown association with difficult birth but not with neonatal diarrhea in addition to other associations. Hypertension during pregnancy recognized to be a potent factor in MR, mild as well as serious cases with other neurological conditions and this information is in line with previous studies (Griffith et al. 2011; Langridge et al. 2013) but many studies did not find any association between this factor and any of subgroups of MR (Bilder et al. 2009, 2013; Griffith et al. 2011; Leonard et al. 2006; Mann et al. 2013). Authors examined the association of neonatal diarrhea with all consecutive ID except serious MR. Neonatal diarrhea is recognized as one of the leading cause of ID (Haworth et al. 2017). The factor which was not found to be associated with either of subgroups is breech delivery (when a baby is born bottom first instead of head), and this information is in line with work done by Durkin et al. in 2000. Maternal tobacco use was found to be associated with cases with other neurological abnormalities (Drews et al. 1996; Langridge et al. 2013; Mann et al. 2013; Roeleveld 1992) but not in isolated cases.

CONCLUSIONS

Results of the present investigation are worth mentioning and may be unexpected to some investigators who have grouped mental retardation only on the basis of IQ scores so more subgroups of persons with MR can be categorized on the basis of presence or absence of other neurological disorders. Affirmation of the association between various risk factors and subgroups of ID/MR bring into being in this study would suggest that public health campaigns may be indicated to inform families at risk. This information can be utilized for an intervention of ID and also emphasize the importance of breaking this cycle, thus filling the gap in the current literature around risk factors of disability in a high burden country.

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Appendices

Table 1: Frequencies of Various Risk Factors in Population Cohorts of Mentally Retarded and Normal Individuals

Variables	Isolated MR (N=63)				MR with Other Neurological Conditions (N=87)				Control (N=150)	
	N	%	χ^2 Value	Sig.	N	%	χ^2 Value	Sig.	N	%
3. Paternal education										
i. <High school	16	25.40	1.10	0.29	24	27.59	0.67	0.41	49	32.67
ii. Graduate	27	42.86	4.86	0.03	38	43.68	5.43	0.02	89	59.33
iii. Post graduate	20	31.74	19.60	<0.001	25	28.73	17.97	<0.001	12	8.00
4. Maternal Education										
i. <High school	43	68.25	23.83	<0.001	59	67.82	28.52	<0.001	48	32.00
ii. Graduate	11	17.47	14.77	<0.001	17	19.54	15.92	<0.001	68	45.33
iii. Post graduate	9	14.28	1.93	0.16	11	12.64	3.60	0.06	34	22.67
Perinatal Factors										
1. Maternal history of pregnacy loss	28	44.44	54.10	<0.001	54	62.07	98.20	<0.001	6	4.00
4. Hypertension during pregnancy	19	30.16	4.38	0.04	28	32.18	6.90	0.009	26	17.33
7. Maternal tobacco use	3	4.76	4.04	0.08*	6	6.89	7.46	0.01*	1	0.67
9. Maternal asthma	4	6.35	1.00	0.45*	10	11.49	6.18	0.01	5	3.33
9. Lack of prenatal care	34	53.97	66.29	<0.001	42	48.27	61.00	<0.001	8	5.33
Perinatal Factors										
2. Breech delivery	2	3.17	0.04	0.84*	6	6.90	2.44	0.18*	4	2.67
3. Difficult birth	12	19.05	3.91	0.05	16	18.39	4.08	0.04	14	9.33
Neonatal Factors										
2. Neonatal Diarrhoea	16	25.40	16.11	<0.001	35	40.23	42.67	<0.001	9	6.00
3. Neonatal infection	24	38.09	39.87	<0.001	45	51.72	71.19	<0.001	7	4.67

Table 2: Association with Mild MR with Potent Risk Factors in Isolated and Cases with Other Neurological Disorders

Variables	Isolated Mild MR (N=53)				Mild MR with Other Neurological Conditions (N=62)				Control (N=150)	
Demographic Factors	N	%	χ^2 Value	Sig.	N	%	χ^2 Value	Sig.	N	%
3. Paternal education										
i. <High school	11	20.75	2.67	0.10	11	17.74	4.82	0.03	49	32.67
ii. Graduate	23	43.40	4.02	0.04	30	48.39	2.13	0.14	89	59.33
iii. Post graduate	19	35.85	23.47	<0.001	21	33.87	22.34	<0.001	12	8.00

Table 2: Contd.,										
4. Maternal Education i. <High school ii. Graduate iii. Post graduate	36 9 8	67.92 16.99 15.09	20.84 13.37 1.37	<0.001 <0.001 0.24	45 9 8	72.58 14.52 12.90	29.34 18.01 2.63	<0.001 <0.001 0.10	48 68 34	32.00 45.33 22.67
Prenatal Factors										
1. Maternal history of pregnacy loss	23	43.40	49.64	<0.001	31	50.00	64.43	<0.001	6	4.00
4. Hypertension during pregnancy	16	30.19	3.94	0.05	24	38.71	11.12	0.001	26	17.33
7. Maternal tobacco use	3	5.66	5.06	0.06*	4	6.45	6.38	0.03*	1	0.67
9. Lack of prenatal care Malnutrition	34	64.15	82.56	<0.001	42	67.74	94.80	<0.001	8	5.33
Perinatal Factors										
2. Breech delivery	2	3.77	0.16	0.65*	4	6.45	1.73	0.24*	4	2.67
3. Difficult birth	2	3.77	1.67	0.25*	4	6.45	0.47	0.59*	14	9.33
Neonatal Factors										
2. Neonatal Diarrhoea	14	26.41	16.25	<0.001	30	48.38	52.50	<0.001	9	6.60
3. Neonatal infection	18	33.96	31.12	<0.001	36	58.06	77.36	<0.001	7	4.67

Table 3: Frequencies and Association of Various Risk Factors in Isolated and Cases with Other Neurological Disorders in Serious Mental Retardation

Variables	Isolated Serious MR (N=10)				Serious MR with Other Neurological Conditions (N=25)				Control (N=150)	
Demographic Factors	**N**	**%**	**χ^2 Value**	**Sig.**	**N**	**%**	**χ^2 Value**	**Sig.**	**N**	**%**
3. Paternal education i. <High school ii. Graduate iii. Post graduate	 5 4 1	 50.00 40.00 10.00	 1.26 1.44 0.05	 0.26 0.32* 0.58*	 13 8 4	 52.00 32.00 16.00	 3.50 6.48 1.65	 0.06 0.01 0.25	 49 89 12	 32.67 59.33 8.00
4. Maternal Education i. <High school ii. Graduate iii. Post graduate	 7 2 1	 70.00 20.00 10.00	 6.00 2.44 0.88	 0.01 0.19* 0.35*	 14 8 3	 56.00 32.00 12.00	 5.40 1.55 1.46	 0.02 0.21 0.30*	 48 68 34	 32.00 45.33 22.67
Perinatal Factors										
1. Maternal history of pregnacy loss	5	50.00	30.53	<0.001	23	92.00	118.6	<0.001	6	4.00
4. Hypertension during pregnancy	3	30.00	1.01	0.39*	4	16.00	0.03	0.87*	26	17.33
7. Maternal tobacco use	1	10.00	6.62	0.12*	2	8.00	6.84	0.05*	1	0.67

Table 3: Contd.,										
9. Lack of prenatal; care	10	10.00	84.15	<0.001	7	28.00	14.05	<0.001	8	5.33
Perinatal Factors										
2. Breech delivery	0	0.00	0.27	0.60*	2	8.00	1.84	0.20*	4	2.67
3. Difficult birth	4	40.00	8.83	0.003	3	12.00	0.17	0.68	14	9.33
Neonatal Factors										
2. Neonatal Diarrhoea	2	20.00	2.87	0.14*	5	20.00	5.70	0.02	9	6.00
3. Neonatal infection	6	60.00	38.45	<0.001	9	36.00	25.32	<0.001	7	4.67

Use of superscript * in some χ^2- values indicates that these are computed using Fischer's exact test modification of χ^2 test due to small sample sizes